Brief Summary of the Circulatory System Devices Panel Meeting – October 8, 2014

Introduction:

The Circulatory System Devices Panel of the Medical Devices Advisory Committee to the Food and Drug Administration met on October 8, 2014 to make recommendations and vote on information related to the premarket approval application regarding Boston Scientific Corporation's WATCHMAN Left Atrial Appendage (LAA) Closure Technology. FDA was seeking committee review and recommendations regarding new clinical data and associated additional adverse events including stroke that have become available since the previous advisory committee meeting on the WATCHMAN device, which was held December 11, 2013.

The sponsor has proposed the following Indications for Use:

The WATCHMAN LAAC Device is indicated to prevent thromboembolism from the left atrial appendage. The device may be considered for patients with non-valvular atrial fibrillation who, based on $CHADS_2$ or CHA_2DS_2-VASc scores, would be recommended for warfarin therapy to reduce the risk of stroke and systemic embolism.

Panel Deliberations/FDA Questions:

Panel Question 1: Evaluation of Device Effectiveness for Reducing Ischemic Stroke

The general consensus of the Panel was that the WATCHMAN device is inferior to warfarin with respect to reducing the risk of ischemic stroke.

Panel Question 2: Evaluation of Hemorrhagic Stroke

The Panel believed that there is still a question as to whether the difference in hemorrhagic stroke rates between the WATCHMAN device and the control reflects an unusually high rate of events in the control group that may have been inflated by the concomitant use of antiplatelet agents. Overall, there appeared to be a difference in hemorrhagic stroke rates between WATCHMAN and warfarin groups that favors the WATCHMAN device, but the magnitude of this difference is small.

Panel Question 3: Updated PREVAIL First and Second Primary Endpoint Results

The Panel was concerned by the fact that the WATCHMAN device did not meet the 1st and 2nd primary endpoints in PREVAIL.

Panel Question 4: Evaluation of Major Bleeding Events

The Panel agreed that bleeding events need to be more rigorously evaluated in the acute peri-procedural period and during follow-up. Several Panel members noted that it would be expected that patients taking warfarin would have more bleeding than the WATCHMAN patients taking aspirin alone. The majority of the Panel did not feel there is a significant difference in overall major bleeding events, but that continued follow-up could reveal a difference in bleeding over time.

Panel Question 5: Proposed Indications For Use

The Panel was uncomfortable with the proposed Indications for Use statement as written and expressed concern over the broad patient population encompassed by the current wording of the statement as well as the implication that the device effectively prevents ischemic stroke and systemic embolism.

Panel Question 6: Evaluation of the Totality of the Data from the WATCHMAN trials

The Panel was unanimous in their opinion that the WATCHMAN device is not appropriate for all warfarin eligible patients but may be considered in those who choose not to or cannot take long-term warfarin.

Panel Question 7: Labeling

Similar to the concerns expressed about the proposed Indications for Use, the Panel was concerned about the current labeling and how patients will be educated on how to make an informed decision when considering the WATCHMAN device as an option vs. warfarin. The Panel again noted that it should be made clear that the device should be considered as a second-line therapy for patients who have major problems taking long-term warfarin.

Panel Question 8: Post-Approval Study

The Panel emphasized the need for a rigorous post-approval study, including close monitoring of the use of the WATCHMAN device if it is approved. Several Panel members suggested a registry may be useful. Ultimately, the Panel would like to ensure that the WATCHMAN device, if approved, is used as a second-line therapy in an appropriate patient population.

Vote:
The panel voted on the safety, effectiveness, and risk benefit ratio of the Boston Scientific WATCHMAN® Left Atrial Appendage Closure Therapy.

On Question 1, the panel voted 12-0 that the data show reasonable assurance that the Boston Scientific WATCHMAN® Left Atrial Appendage Closure Therapy is safe for use in patients who meet the criteria specified in the proposed indication.

On Question 2, the panel voted 6-7 (chair voted in tie breaker) that there is reasonable assurance that the Boston Scientific WATCHMAN® Left Atrial Appendage Closure Therapy is effective for use in patients who meet the criteria specified in the proposed indication.

On Question 3, the panel voted 6-5 (1 abstain) that the benefits of the Boston Scientific WATCHMAN® Left Atrial Appendage Closure Therapy outweigh the risks for use in patients who meet the criteria specified in the proposed indication.

Several panelists noted that part of their positive vote was based on anticipation of a more limited, revised indication, or that they would have voted positively had the indication been limited to a more specific patient population.

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